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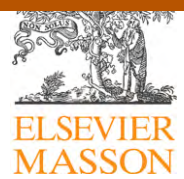

CLINICAL RESEARCH

Distribution of left ventricular ejection fraction and heart rate values in a cohort of stable coronary patients: The INDYCE registry

Distribution de la fraction d'éjection ventriculaire gauche et de la fréquence cardiaque de repos dans une cohorte de patients coronariens stables : le registre INDYCE

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KEYWORDS
Coronary artery disease;
Angina;
Left ventricular ejection fraction;
Heart rate

Summary
Background. — The distribution of left ventricular ejection fraction (LVEF) — a key factor in coronary artery disease (CAD) patient management and prognostication — is poorly documented.
Objective. — To determine LVEF and heart rate (HR) values, and describe the management of stable CAD patients in France.
Methods. — The INDYCE survey was a prospective, multicentre registry of consecutive stable CAD outpatients attending a cardiology consultation. The survey focused on LVEF values measured using the echocardiographic Simpson biplane method. Drug therapy, resting HR, blood pressure and symptoms were also recorded.

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Results. — Overall, 3119 patients (68.4 ± 11.0 years; 80% men) were enrolled. LVEF was 56.1 ± 11.8% on average, and was poor (< 40%) and moderately impaired (40—50%) in 9.6% ($n = 298$) and 19.8% ($n = 619$) of cases, respectively. Symptomatic angina pectoris was present in 19.2% of cases and only 40.6% of patients were asymptomatic (no angina and NYHA class ≤ I) despite relatively aggressive management (79.0% of patients had undergone coronary angioplasty and/or bypass graft). Interestingly, 14.1% of patients with LVEF less than 40% were asymptomatic. In multivariable analysis, LVEF less than 40% was associated most strongly with symptomatic status (odds ratio 3.82; 95% CI 2.59—5.63; $P < 0.0001$), together with female sex, age greater than 75 years, diabetes, HR greater or equal to 70 bpm, sedentariness, obesity and disease duration.

Conclusion. — Only 9.6% of stable CAD patients had severe left ventricular dysfunction; among them, 14.1% were strictly asymptomatic. This could justify regular LVEF measurement in CAD patients. Three potentially reversible factors (HR ≥ 70 bpm, being overweight and sedentariness) were linked independently to the presence of symptoms.

MOTS CLÉS
Cardiopathie ischémique ;
Angor ;
Fraction d'éjection ventriculaire gauche

Résumé

État des lieux. — La prise en charge et l'évaluation du pronostic des patients coronariens stables sont en grande partie basées sur la fraction d'éjection ventriculaire gauche (FEVG), mais la distribution de celle-ci chez ces patients est peu documentée.

Objectifs. — Décrire la distribution des valeurs de FEVG et de fréquence cardiaque de repos (Fc) ainsi que la prise en charge des patients coronariens stables en France.

Méthodes. — Le registre INDYCE multicentrique et prospectif a inclus consécutivement les patients coronariens stables vus en consultation externe de cardiologie. L'objectif principal était la mesure de la FEVG par la méthode de Simpson Biplan. Le traitement, la Fc, la pression artérielle et la symptomatologie étaient aussi analysés.

Résultats. — Au total, 3119 patients (âge moyen : 68,4 ± 11,0 ans ; 80 % d'hommes) ont été inclus. La FEVG était de 56,1 ± 11,8 % ; la fonction systolique ventriculaire gauche était sévèrement (FEVG < 40 %) ou modérément (40—50 %) altérée chez respectivement 9,6 % ($n = 298$) et 19,8 % ($n = 619$) des patients. Le pourcentage de patients qui souffraient d'angor était de 19,2 % et seulement 40,6 % d'entre eux étaient strictement asymptomatiques (pas d'angor et classe NYHA ≤ 1) malgré une prise en charge assez agressive (79,0 % des patients ayant bénéficié d'au moins une procédure de revascularisation). On note que 14,1 % des patients avec une FEVG inférieure à 40 % étaient asymptomatiques. En analyse multivariée, l'existence d'une FEVG inférieure à 40 % était le facteur le plus fortement associé à l'existence de symptômes (OR 3,82 ; IC 95 % : 2,59 à 5,63 ; $p < 0,0001$), les autres paramètres étant le sexe féminin, l'âge supérieur à 75 ans, le diabète, une Fc supérieure ou égale à 70 bpm, la sédentarité, l'obésité et l'ancienneté de la maladie angineuse.

Conclusion. — Le pourcentage de patients coronariens stables présentant une dysfonction ventriculaire gauche sévère est de 9,6% ; parmi eux, 14,1 % sont strictement asymptomatiques, ce qui pourrait justifier une mesure régulière de la FEVG chez l'ensemble des coronariens. Seulement trois facteurs potentiellement réversibles (obésité, sédentarité et Fc ≥ 70 bpm) sont associés à l'existence de symptômes.

Abbreviations

bpm	beats per minute
CAD	coronary artery disease
HR	heart rate
LVEF	left ventricular ejection fraction
NYHA	New York Heart Association
OR	odds ratio

Background

Discovery of systolic left ventricular dysfunction is a key event in the course of stable coronary artery disease (CAD). Indeed, it worsens the prognosis [1,2] and often requires changes in patient management, including escalation of medical therapy and reassessment of the need for revascularization.

As systolic left ventricular dysfunction is asymptomatic in 50—65% of cases [3,4], especially when only moderate, there is a strong likelihood that the myocardial impairment will only be diagnosed when already severe and irreversible [5]. The prevalence of systolic left ventricular dysfunction — especially that of moderate forms in patients with stable CAD — is poorly known. Most data come from the Euro Heart Survey [6,7], in which left ventricular ejection fraction (LVEF) was greater than 50% in 66% of CAD patients, between 40% and 50% in 23% of CAD patients, and less than

40% in 11% of CAD patients. However, these data must be interpreted with care, as LVEF was measured in only two-third of the study population. In addition, the prevalence of symptoms in CAD patients receiving the most modern treatments is poorly documented.

The main objective of the INDYCE (*insuffisance coronaire stable, dysfonction ventriculaire gauche et fréquence cardiaque*) registry was to evaluate systolic left ventricular function prospectively in a large population of patients with stable CAD. Secondary objectives were to examine patient management, symptoms and heart rate (HR) distribution.

Methods

This prospective, cross-sectional, epidemiological survey was conducted in France. As it was an observational study, it entailed no change in standard patient management. In keeping with French law, all data were collected anonymously and the data file was declared to the French computer watchdog body (Commission nationale de l'informatique et des libertés). The patients were given written information on the nature and aims of the study.

Patients

The study population consisted exclusively of ambulatory patients seen at a hospital or private cardiology consultation. Between 15 June and 31 October 2008, each investigator was asked to recruit prospectively a maximum of 10 consecutive patients with stable CAD.

Patients were eligible if they were greater or equal to 18 years of age and had documented CAD (history of coronary revascularization and/or coronary angiography showing ≥ 1 stenosis > 60%), and/or a history of myocardial infarction or an acute coronary syndrome, and/or clinical angina and a positive ischaemia test (with the exception of an conventional exercise test in women).

Stable CAD was defined by the absence of acute coronary events and myocardial revascularization during the 6 months before inclusion.

Data collection

Echocardiography

LVEF was measured using the Simpson biplane method [8,9]. An illustrated technical file describing the technique precisely was provided to each investigator.

Clinical data

The monthly number of angina attacks was recorded, and dyspnoea was scored using the New York Heart Association (NYHA) classification. Blood pressure and HR were measured after a 5-minute rest in the supine position; HR was measured from the pulse.

Statistical analysis

Continuous variables are expressed as means ± standard deviations and categorical variables as percentages. Proportions were compared between groups using the Khi^2 test. Overall comparisons between LVEF groups were performed using a one-way analysis of variance model for continuous variables and a Khi^2 test or Fisher's exact test for categorical variables.

Baseline characteristics were tabulated according to three prespecified ejection fraction strata (< 40%, 40—50%, and > 50%), as used in the ECHOES study [3]. As recent data suggest that HR greater or equal to 70 beats per minute (bpm) has a strong prognostic influence on coronary events [10,11], HR values were dichotomized at 70 bpm.

Factors correlating with symptomatic status (i.e. angina attacks and/or NYHA class > I) were identified using univariate and multivariable logistic regression models. Factors that were significant ($\alpha \leq 0.05$) in the univariate analysis were included in the multivariable model, using a stepwise procedure with an entry threshold of 0.10 and an exit threshold of 0.05.

Results

Between June and November 2008, 3193 patients with stable CAD were enrolled consecutively. Seventy-four patients (2.3%) were excluded, because of missing data ($n = 5$), non-distribution of written information ($n = 4$) or non-respect of inclusion criteria ($n = 65$). This analysis focuses on the remaining 3119 patients.

Recruiting centres

Among 979 cardiologists selected by the National Collegiate of French Cardiologists, 554 agreed to participate in the study and 343 actually participated. The demographic characteristics of the cardiologists were similar to those of the 6121 cardiologists practising in France in 2007, based on data from Direction de la récherche des études et de l'évaluation statistique and Observatoire national de la démographie des professions de santé [12].

Patients

Table 1 shows the patients' general characteristics. Most of the patients were men (80.3%). The mean age was 68 ± 11 years. Risk factors and comorbidities occurred frequently: nearly one-quarter of the patients were diabetic, 61.6% were hypertensive, 18.6% were active smokers; two-third were overweight and 28.5% also had extracoronary arterial disease.

The mean CAD duration was 7.6 ± 6.5 years and was frequently severe: 44.5% of the patients had a history of myocardial infarction, 79.0% had been revascularized (angioplasty 61.9%, bypass grafting 24.5%) and 15.2% had been hospitalized at least once for heart failure.

Left ventricular ejection fraction distribution

The distribution of LVEF values is shown in Table 1 and Fig. 1. Mean LVEF was 56.1 ± 11.8%, and was greater than 50% in 70.6% of patients ($n = 2202$), 40—50% in 19.8% of patients ($n = 619$), and less than 40% in 9.6% of patients ($n = 298$).

Table 1 Coronary artery disease risk factors, comorbidity and severity of the disease.

	Total population ($n = 3119$)	LVEF > 50% ($n = 2202$)	LVEF 40—50% ($n = 619$)	LVEF < 40% ($n = 298$)	*P*
Age (years)	68.4 ± 11.0	67.8 ± 10.9	69.5 ± 11.0	70.5 ± 11.7	< 0.0001
Men	80.3	79.4	84.2	78.2	0.021
Insulin-dependent diabetes	5.6	4.5	6.5	11.5	< 0.0001
Non-insulin-dependent diabetes	18.7	17.7	22.3	18.6	0.037
Hyperlipidaemia	81.8	81.5	83.7	80.4	0.369
High blood pressure	61.6	63.4	59.4	53.4	0.002
Familial coronary artery disease	25.0	25.4	23.6	24.8	0.671
Current smoking	18.6	18.6	18.1	19.5	0.882
Peripheral vascular disease	28.5	26.4	31.7	37.5	< 0.0001
Sedentariness	57.4	54.3	62.7	68.8	< 0.0001
Asthma	3.9	3.9	3.2	5.6	0.229
COPD	9.5	8.4	9.5	17.6	< 0.0001
Chronic renal failure	13.9	10.2	18.0	33.3	< 0.0001
Depression	21.4	20.2	21.2	30.1	< 0.001
Body mass index	26.9 ± 4.0	26.9 ± 3.9	27.1 ± 3.9	26.4 ± 4.4	0.037
Duration of coronary artery disease (years)	7.6 ± 6.5	6.9 ± 5.9	8.7 ± 7.2	10.4 ± 8.1	< 0.0001
Prior myocardial infarction	44.5	35.4	63.7	72.2	< 0.0001
Resting heart rate	64.5 ± 10.4	64.0 ± 10.1	65.3 ± 10.7	66.2 ± 11.5	< 0.001
Heart rate ≥ 70 beats per minute	30.1	27.9	33.5	38.6	< 0.001
Systolic blood pressure (mmHg)	131.8 ± 15.4	132.9 ± 14.9	130.7 ± 15.5	125.4 ± 16.3	< 0.0001
Diastolic blood pressure (mmHg)	75.8 ± 8.4	76.2 ± 8.2	75.1 ± 8.4	73.9 ± 9.1	< 0.0001
Sinus rhythm	90.1	92.3	86.6	80.8	< 0.0001
LVEF (%)	56.1 ± 11.8	62.2 ± 6.9	45.9 ± 3.4	32.3 ± 5.9	< 0.0001
Left atrium area (cm^2)	20.4 ± 6.0	19.6 ± 5.4	21.8 ± 6.9	23.8 ± 6.7	< 0.0001
NYHA class					< 0.001
0 or I	43.6	50.8	31.9	14.8	
II	46.9	44.0	54.0	53.4	
III or IV	9.6	5.3	14.2	31.9	
Angina (≥ 1 crisis/month)	19.2	16.7	23.6	29.7	< 0.001
Asymptomatic patients (NYHA class 0 or I and no angina)	40.6	47.3	29.4	14.1	< 0.001
Prior hospitalization for heart failure	15.2	6.7	24.8	58.7	< 0.0001

Data are mean ± standard deviation or percentage. COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

Univariate regression analysis followed by multivariable analysis was used to determine if demographic factors (age, sex), clinical characteristics (diabetes, smoking, family history of CAD, lipid disorders, obesity, systolic pressure, HR, prior myocardial infarction, disease duration), treatments (history of bypass grafting or angioplasty) and symptomatic status of the patients were linked independently to LVEF less than 40%. Finally, age greater than 75 years (odds ratio [OR] 1.36), HR greater or equal to 70 bpm (OR 1.53), disease duration greater or equal to 6 years (OR 1.57), previous myocardial infarction (OR 2.96), absence of myocardial revascularization (OR 1.56), high blood pressure (OR 0.60), and presence of symptoms (angina and/or NYHA class > I) (OR 3.76) were linked independently with severe left ventricular dysfunction (Table 2).

Heart rate distribution

The mean resting HR was 64.5 ± 10.4 bpm (Table 1 and Fig. 2). The mean HR in the 74.6% of patients who were taking beta-blockers was 63.3 ± 9.9 bpm, compared with 68.0 ± 10.9 bpm in the other patients ($P < 0.0001$). HR was greater or equal to 70 bpm in 30.1% of patients overall, and in 25.4% and 43.7% of patients taking and not taking beta-blockers, respectively. HR-lowering calcium antagonists were prescribed to only 9.0% of the patients overall, and to 32.2% of the patients who were not taking a beta-blocker.

Symptoms

Overall, 19.2% of patients had at least one angina attack per month; 40.6% of patients were considered completely

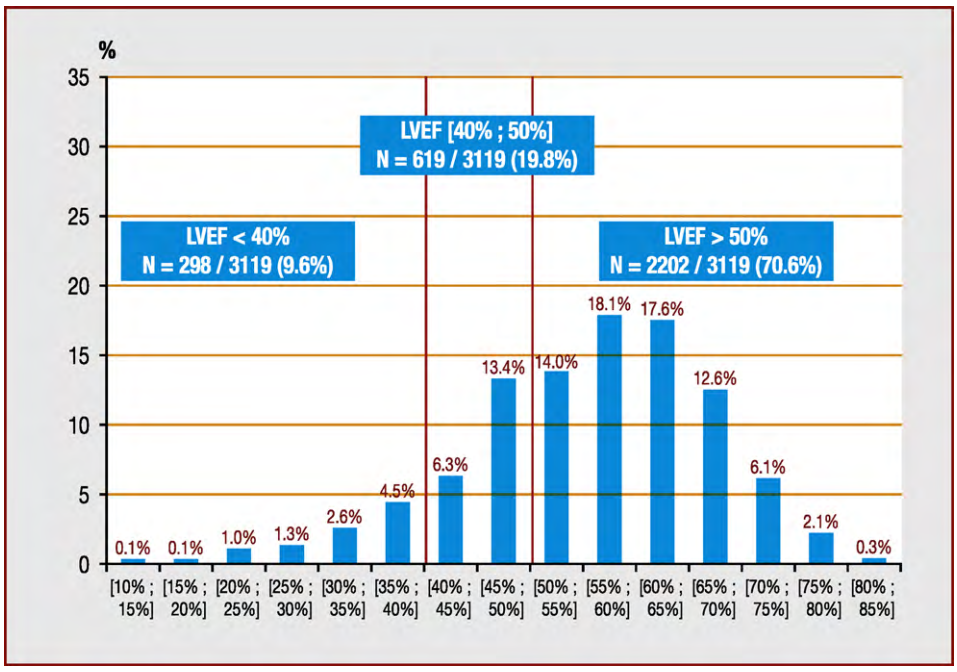

Figure 1. Left ventricular ejection fraction (LVEF) distribution.

asymptomatic (NYHA class 0 or I, and no angina). Interestingly, 14.1% of patients with LVEF less than 40% were asymptomatic.

Univariate regression analysis followed by multivariable analysis was used to identify demographic factors (age, sex), clinical characteristics (diabetes, smoking, family history of CAD, lipid disorders, obesity, systolic pressure, HR, prior myocardial infarction, disease duration), paraclinical variables (LVEF) and treatments (history of bypass grafting or angioplasty) that were linked independently to the presence of symptoms.

Age greater than 75 years (OR 2.52), female sex (OR 1.44), obesity (body mass index $\geq$ 30) (OR 1.50), diabetes

Table 2 Factors linked to the presence of a left ventricular ejection fraction less than 40%.

Criteria	Univariate analysis		Multivariable analysis	
	χ^2	*P*	*P*	Odds ratio (95% CI)
Age > 75 years	19	< 0.0001	0.03	1.36 (1.02—1.80)
Body mass index $\geq$ 30	0.8	0.3		
Heart rate $\geq$ 70	11	< 0.001	0.003	1.53 (1.15—2.03)
Male sex	0.8	0.36		
Sedentariness	17	< 0.0001	0.25	1.18 (0.88—1.57)
Disease duration $\geq$ 6 years	35	< 0.0001	0.002	1.57 (1.18—2.09)
Diabetes	5.5	0.02	0.57	1.09 (0.80—1.48)
Previous myocardial infarction	93	< 0.0001	< 0.0001	2.96 (2.20—3.99)
Previous revascularization	14	0.002	0.001	0.64 (0.49—0.84)
Current smoking	0.2	0.6		
Family history of coronary artery disease	0.01	0.9		
Dyslipidaemia	0.3	0.5		
High blood pressure	56	< 0.0001	< 0.001	0.60 (0.45—0.80)
Beta-blocker therapy	5.8	0.02	0.9	1.02 (0.71—1.45)
Calcium antagonist therapy	14.5	0.001	< 0.0001	0.25 (0.16—0.40)
Symptomatic (NYHA class > I and no angina)	72	< 0.0001	< 0.0001	3.76 (2.55—5.55)
ACEI or ARB therapy	27	< 0.0001	< 0.0001	3.80 (2.45—5.90)
Anti-ischaemic therapy (nitrates, nicorandil, trimetazidine)	16.3	0.009	0.06	1.36 (0.98—1.87)

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CI: confidence interval; NYHA: New York Heart Association.

Table 3 Factors linked to the presence of symptoms (angina and/or New York Heart Association class > I).

Criteria	Univariate analysis		Multivariable analysis	
	χ^2	*P*	*P*	Odds ratio (95% CI)
Age > 75 years	146	< 0.0001	< 0.0001	2.52 (2.05—3.09)
Body mass index ≥ 30	29	< 0.0001	< 0.001	1.50 (1.20—1.87)
Heart rate ≥ 70	25	< 0.0001	0.02	1.25 (1.03—1.51)
Female sex	42	< 0.0001	0.001	1.44 (1.14—1.81)
Sedentariness	158	< 0.0001	< 0.0001	2.14 (1.81—2.55)
LVEF < 40%	72	< 0.0001	< 0.0001	3.82 (2.59—5.63)
Disease duration ≥ 6 years	30	< 0.0001	0.006	1.28 (1.07—1.52)
Diabetes	43	< 0.0001	< 0.001	1.47 (1.19—1.82)
Previous myocardial infarction	1.2	0.33		
Previous revascularization	2.8	0.01	0.09	0.86 (0.72—1.02)
Current smoking	5.4	0.02	0.75	0.99 (0.81—1.22)
Family history of coronary artery disease	1.9	0.1		
Dyslipidaemia	1.4	0.2		
High blood pressure	15	0.02	0.07	1.03 (0.99—1.06)
Beta-blocker therapy	4.5	0.03	0.006	1.32 (1.08—1.60)
Calcium antagonist therapy	3.2	0.053		
ACEI or ARBS therapy	16.3	< 0.0001	0.028	1.24 (1.02—1.50)
Anti-ischaemic therapy (nitrates, nicorandil, trimetazidine)	37	< 0.0001	< 0.0001	1.96 (1.55—2.49)

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CI: confidence interval; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

(OR 1.47), HR greater or equal to 70 bpm (OR 1.25), sedentariness (OR 2.14), disease duration greater than 6 years (OR 1.28) and LVEF less than 40% (OR 3.82) were associated independently with symptomatic status (Table 3).

Management

Patient management (Table 4) was relatively aggressive (91.5% of patients had a history of coronary angiography and 79.0% had undergone coronary bypass grafting and/or coronary angioplasty). Drug therapy was largely in keeping with contemporary guidelines: 91.0% of patients were receiving antiplatelet therapy, 85.9% a statin, 71.5% an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and 74.6% a beta-blocker. Only 44.7% of patients were receiving a combination of a beta-blocker, a statin, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and an antiplatelet drug, while 29.8% of patients were receiving all these treatments and had well-controlled blood pressure (systolic < 140 mmHg and diastolic < 90 mmHg). Only 23% of patients were receiving the combination of the above four drugs and had well-controlled blood pressure and an HR less than 70 bpm.

A total of 9.9% of patients were not receiving any antiangina drug therapy (beta-blockers, calcium antagonists, nitrate derivatives and related drugs, trimetazidine or ivabradine), while 61.8%, 23.1%, 4.6% and 0.6% of patients were receiving one, two, three or four antiangina drugs, respectively.

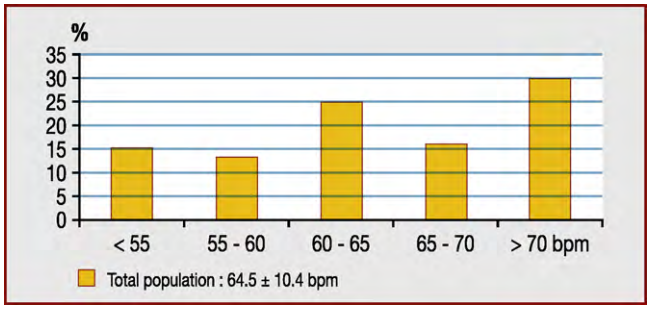

Figure 2. Heart rate distribution. Heart rate was greater or equal to 70 bpm in 30% of patients overall, in 25.4% of patients on beta-blockers and in 43.7% of patients not on beta-blockers. bpm: beats per minute.

Discussion

In some respects, patients with stable CAD are poorly characterized. Large clinical studies of such patients [10,13—18], designed to validate specific treatments or management strategies, have been useful, but the study populations were not representative of patients seen in routine practice: for example, patients with left ventricular dysfunction were excluded from the PEACE study [14], while patients with normal left ventricular function were excluded from the BEAUTIFUL study [15].

Some large registries, such as the Euro Heart Survey [6,7] and the French ELAN study [19], provide a more comprehensive picture of the clinical features and management of these patients, but their results are incomplete. In partic-

Table 4 Management and medical therapy.

	Total population ($n = 3119$)	LVEF > 50% ($n = 2202$)	LVEF 40—50% ($n = 619$)	LVEF < 40% ($n = 298$)	*P*
Prior coronary angiography	91.5	92.3	89.8	88.9	0.035
Prior PCI	61.9	65.2	55.7	51.0	< 0.0001
Prior CABG	24.5	23.1	26.7	29.9	0.014
Antiplatelet agent	91.0	93.4	89.0	77.5	< 0.001
Aspirin	54.5	53.9	57.5	52.0	0.51
Clopidogrel	23.6	24.1	21.2	24.7	0.51
Aspirin + clopidogrel	22.0	22.0	21.2	23.4	0.51
VKA	10.8	7.5	13.9	28.9	< 0.001
Statin	85.9	87.3	84.0	79.5	< 0.001
Other lipid-lowering agent	8.1	8.2	8.2	6.7	0.67
ACEI	49.3	43.5	60.7	67.8	< 0.001
ARB	23.5	23.0	24.6	25.2	0.57
ACEI and/or ARB	71.5	65.1	84.1	91.9	< 0.01
Beta-blocker	74.6	72.8	78.4	80.5	
> 125% of target dose	3.2	3.4	3.1	2.1	
75—125% of target dose	35.8	37.0	23.2	35.4	
50—75% of target dose	36.7	39.1	33.4	27.5	
25—50% of target dose	18.4	15.6	24.3	25.4	
< 25% of target dose	5.8	4.9	7.0	9.6	
Mean dose (% of target dose)	67.1 ± 46.8	69.6 ± 49.8	62.6 ± 40.0	59.7 ± 36.8	< 0.001
Nitrate	7.6	6.9	7.8	12.8	0.001
Nicorandil	8.5	9.1	7.0	7.4	0.174
Trimetazidine	5.0	5.0	4.2	7.1	0.180
Dihydropyridine	19.4	21.9	16.6	6.7	< 0.001
Non-dihydropyridine calcium antagonist	9.0	10.6	6.5	2.4	< 0.001
Beta-blocker + AA + ACEI/ARB + statin	44.7	41.5	53.3	50.3	< 0.001

Data are mean ± standard deviation or percentage. The beta-blocker dose is expressed as a percentage of the target dose (bisoprolol, 10 mg; acebutolol, 400 mg; atenolol, 100 mg; celiprolol, 400 mg; metoprolol, 200 mg) [25]. AA: antiplatelet agent; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention; VKA: vitamin K antagonist.

ular, we are not aware of any studies focusing on systolic left ventricular function in patients with stable CAD, even though this is the most potent prognostic factor [20]. Furthermore, the prognostic significance of HR (especially for coronary events), with a cut-off of 70 bpm, was discovered only recently. The INDYCE registry provides precise data on the distribution of these two variables in ambulatory patients with stable CAD managed routinely by cardiologists.

Our results are particularly interesting. Indeed, while the systolic left ventricular function of these patients with stable CAD was generally good (mean LVEF 56.1 ± 11.8%), LVEF was less than 50% in 29.4% of patients and less than 40% in 9.6% of patients. It is noteworthy that 70.3% of the patients with severe left ventricular dysfunction (LVEF < 40%) were free of angina and that 14.1% were completely asymptomatic. This confirms that changes in systolic left ventricular function can proceed silently in this setting, and supports the use of regular echocardiographic monitoring, although the optimal interval remains to be determined.

Management of our patients complied largely with contemporary guidelines, especially with respect to drug therapy; in particular, nearly three-quarter of patients were receiving beta-blockers — a higher proportion than in the Euro Heart Survey (67%) [7] or in the recent LHYCORNE study (62%) [21]. Moreover the mean beta-blocker dose was superior to that observed in the last French survey focusing on this topic, where it was close to 50% of the theoretical dose [22].

Closer examination of the data shows that there is still room for improvement. Indeed, management could be considered optimal in only one-quarter of cases, being based on a beta-blocker, an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, a statin and an antiplatelet drug, with good control of arterial pressure and HR less than 70 bpm.

Interestingly, three potentially reversible factors were linked independently to the presence of symptoms, namely obesity, lack of physical exercise and HR greater or equal to 70 bpm. These variables may be suitable targets for intervention, rather than serving merely as gravity signs. Indeed,

exercise and weight loss are both associated with better outcome [20], and the analysis of the BEAUTIFUL study [15] suggests that slowing of HR reduces the risk of myocardial infarction, especially in patients with angina [23].

Limitations

The main weakness of the INDYCE registry is that the echocardiographic results were not centralized for reanalysis. However, differences between LVEF values determined in a core laboratory and in individual investigating centres are usually minimal [24]; moreover, in real life, clinical decisions are taken without any centralization of echocardiographic findings. Finally, as INDYCE is a registry, it was not possible to evaluate treatment efficacy: for instance, the correlation between administration of beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and anti-ischaemic therapy and the presence of symptoms (Table 3) should not be misunderstood — these treatments are given because of the existence of symptoms, they do not worsen them.

Conclusion

LVEF is generally preserved in stable CAD patients. However, changes in systolic left ventricular function can proceed silently in this setting. This supports the use of regular echocardiographic monitoring, although the optimal interval remains to be determined. Three potentially reversible factors (HR $\geq$ 70 bpm, being overweight and sedentariness) are linked independently to the presence of symptoms.

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Conflict of interest statement

Philippe Meurin is a scientific advisor for Servier.

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